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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/732,954	12/11/2003	Alexander Sulakvelidze	62610.000043	9240

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HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER
KINSEY WHITE, NICOLE ERIN

ART UNIT	PAPER NUMBER
1648	

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08/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/732,954	SULAKVELIDZE ET AL.	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *110-122 and 125-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *110-122 and 125-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 110-115 and 125-128 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. (EP 0 414 304 A2).

The claims are drawn to a method of sanitizing a hard surface contaminated by a bacterial species and located in an area accessed by immunocompromised patients comprising: (a) providing a hard surface located in an area accessed by immunocompromised patients; (b) providing a composition consisting essentially of at least one bacteriophage that targets said bacterial species, wherein the bacteriophage

concentration is 10^5-10^{11} PFU/ml; (c) applying the composition to the hard surface; and (d) reducing the microbial count of said bacterial species on the hard surface by at least about one log.

Jones et al., discloses a method for sanitizing a hard surface comprising providing a hard surface, providing a composition comprising at least one bacteriophage at a concentration of 10^2 particles/ml, but preferably more than 10^3 particles/ml, applying the composition to the surface and significantly reducing the microbial count (see abstract and col. 6, lines 17-28).

Jones et al. further discloses that the bacteriophage can be used to clean a hard surface such as a toilet bowl. It is common knowledge that toilet bowls and other hard surfaces are located in hospitals where patients, including immunocompromised patients (AIDS patients, organ transplant patients, patients undergoing chemotherapy), receive treatment. It is also common knowledge that hospitals notoriously have problems with nosocomial infections due to poor infection-control policies.

Regarding applicants' claimed range of 10^5-10^{11} PFU/ml, according to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally

known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, Jones et al. produced a recognized result (i.e., significant reduction of bacteria on a hard surface, Examples 1-7). Therefore, determining other optimum or workable concentrations is routine experimentation.

Response to Arguments

In the reply filed on May 7, 2008, applicants argue that Jones teaches a composition comprising bacteriophage and a surfactant and that the surfactant i) must be present and ii) materially affects the characteristics of the composition. Applicants cite Hagens to support their argument that phage concentration is critical. Applicants' arguments have been fully considered, but not found persuasive.

As stated above, Jones et al. teaches an antibacterial composition comprising bacteriophage and a surfactant. The active ingredient is bacteriophage, not the surfactant. This is evidenced by col. 3, lines 24-29, which states "[a]n important function of the surfactant is that it helps to wet the surface, so that the composition is properly distributed over the entire surface. Another function is of course that the surfactant helps to solubilise and remove dirt so that bacterial [sic] become accessible." This does

not teach or suggest that the surfactant is a critical component that materially affects the characteristics of the composition, as argued by applicants. In fact, the bacteriophage are solely responsible for reducing/killing the bacteriophage, not the surfactant. This is supported by Examples 1-7. Jones states that "an aqueous composition was prepared containing 10^3 particles of a bacteriophage against *E. coli*, 1% Tween 80 and 0.01% sodium chloride. The composition was stored for two months at room temperature and it was found that the infectivity was essentially unchanged. The above composition was brought into contact with a ceramic tile coated with a layer of *E. coli* cells. After treatment with the composition containing phage the *E. coli* on the tile was significantly reduced, the composition without phage did not have this effect" (emphasis added) (see column 6, lines 17-28). Jones established i) that a composition comprising10^3 particles is effective and ii) that the bacteriophage alone are responsible for the reduction of bacteria on the hard surface, not the surfactant. Thus, the composition of Jones et al. consists essentially of bacteriophage.

Claims 116-122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones et al. as applied to claims 110-115 and 125-128 above, and further in view of Holzman (Genetic Engineering News, 1998, 18(18):1), Boyce et al. (Journal of Clinical Microbiology, 1994, 32(5):1148-1153) and Cox et al. (Poultry Science, 1990, 69:1606-1609).

The claims are drawn to a method of sanitizing equipment contaminated by a bacterial species comprising: (a) providing equipment; (b) providing a composition

consisting essentially of at least one bacteriophage that targets said bacterial species, wherein the bacteriophage concentration is 10^5-10^{11} PFU/ml; (c) applying the composition to the equipment; and (d) reducing the microbial count of said bacterial species on the equipment by at least about one log.

The teachings of Jones et al. are outlined above.

Jones et al. does not teach using bacteriophage to target resistant bacteria nor sanitizing equipment.

Holzman teaches the use of phages to treat multi-drug resistant bacteria and vancomycin-resistant enterococci (VRE) (see pages 1 and 12). Holzman also discloses that hospitals are experiencing outbreaks of VRE (Other scientists pointed out the need for hospitals to examine their infection-control practices. According to William Martone, M.D., senior executive director, National Foundation for Infectious Diseases, once the first outbreaks of vancomycin-resistant enterococci (VRE) were reported in the mid-1980s, experts realized that the pathogen would eventually spread throughout hospitals. Indeed, since that time, reports of VRE have increased 20-fold.) (see page 12). Further, Holzman states that "VRE accounts for about 25% of nosocomial blood stream infections by enterococcus, approximately 30 cases a month here at the University of Maryland Medical System."

Boyce et al. teaches that when VRE affected patients had no diarrhea, nearly all hospital environmental isolates were obtained from patient gowns, bed linens, or bed side rails. In contrast, when affected patients had diarrhea, hospital environmental isolates were obtained from intravenous pumps, electrocardiogram monitors, overbed

tables, floors, a blood pressure cuff, pulse-oximeter coupling, stethoscope, and bathroom doors (see, for example, page 1151, left column).

Cox et al. teaches that equipment in poultry hatcheries is contaminated with *Salmonella* (*Salmonella* contamination was found on egg shells, pads and equipment such as conveyor belts).

It would have been obvious to one of ordinary skill in the art to modify the method taught by Jones et al. and apply bacteriophage (e.g., bacteriophage that target resistant bacteria) to any hard surface (including equipment and surfaces in hospitals) that could be contaminated or come in contact with bacteria, e.g., resistant bacteria, to sanitize or reduce bacteria on that surface. One would have been motivated to do so given the suggestions of Holzman et al. (phage can be used to treat multi-drug resistant bacteria and VRE, and hospitals have problems with the spread of resistant bacteria), Boyce et al. (VRE isolates are obtained from multiple surfaces in hospitals) and Cox et al. (equipment in hatcheries is contaminated with bacteria). There would have been a reasonable expectation of success given the common knowledge that undesirable microbes exist in bathrooms, kitchens, hospitals and public areas and that bacteriophages kill these microbes (see Jones et al. and Holzman). It is also common knowledge that bacteria and other microbes are easily transferred from one surface to another via contact with an infected source, hence the availability of bleach or other antibacterial/antimicrobial products sold in stores for use in disinfecting kitchens and bathroom surfaces.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In the reply filed on May 7, 2008, applicants argue that Jones does not teach the claimed composition and that the secondary references do not teach sanitizing surfaces or equipment with bacteriophage. Applicants' arguments have been fully considered, but not found persuasive.

It appears applicants are addressing each reference separately instead of the combined teachings of the references. As detailed above, Jones teaches the use of bacteriophage to sanitize a hard surface. The remaining secondary references teach that bacteria are found in hospitals (drug resistant bacteria) and in poultry hatcheries (*Salmonella*) on various hard surfaces. Holzman teaches the use of phages to treat multi-drug resistant bacteria and that hospitals are experiencing outbreaks of VRE. Boyce et al. teaches that resistant bacteria isolates were obtained from hard surfaces such as intravenous pumps, electrocardiogram monitors, overbed tables, floors, a blood pressure cuff, pulse-oximeter coupling, stethoscope, and bathroom doors, and Cox et al. teaches that equipment in poultry hatcheries is contaminated with *Salmonella* (*Salmonella* contamination was found on egg shells, pads and equipment such as conveyor belts). The combined teachings, as outlined above, teach each limitation of the claims and provide the requisite motivation and reasonable expectation of success. Thus, the combined teachings render the claimed invention obvious to one of ordinary skill in the art.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nicole Kinsey White, PhD/
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648